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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/586,879	07/21/2006	Masako Nakazawa	293592US0PCT	8110

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EXAMINER	
PAGONAKIS, ANNA	
ART UNIT	PAPER NUMBER
1628	

NOTIFICATION DATE	DELIVERY MODE
12/23/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/586,879	NAKAZAWA ET AL.	
	Examiner	Art Unit	
	ANNA PAGONAKIS	1628	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *3/8/2010 & 4/1/2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4 and 6-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-2, 4 and 6-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office Action has been withdrawn pursuant to 37 CFR 1.114. Applicant's payment and submission filed 4/1/2010 has been received and entered into the present application. Accordingly, prosecution has been reopened.

Applicant's amendment filed 3/8/2010 have been received and entered into the present application.

Applicant's arguments filed 3/8/2010 have been fully considered. Rejections not reiterated from previous Office Actions are hereby withdrawn. The following rejections are either reiterated or newly applied. They constitute the complete set of rejections presently being applied to the instant application.

Status of Claims

Claims 1-2, 4 and 6-25 are currently under examination and the subject matter of the present Office Action.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-2, 4 and 6-25 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Present claim 1, and the claims dependent therefrom, reads upon an injectable aqueous solution preparation having a pH from 2 to 5, the preparation comprising water and the following compounds (A) and (B): (A) 7-ethyl-10-piperidinopiperidinocarbonyloxycamptothecin and (B) acetic acid and sodium

acetate that solubilize 7-ethyl-10-piperidinopiperidinocarbonyloxycamptothecin in the aqueous solution of the acetic acid and sodium acetate at a pH of 2 to 5.

Instant claims 1-3, are directed to non-statutory subject matter because the claims are clearly intended to encompass a product and a process. Specifically, claim 1 recites limitations clearly directed to a product, i.e. an injectable aqueous solution preparation but then goes on to state limitations that are clearly directed to a process, i.e. solubilizing of 7-ethyl-10-piperidinopiperidinocarbonyloxycamptothecin. Accordingly, it seems that Applicant intends to claim a product and process. The overlap between the two statutory categories of invention (i.e., product and process) renders the subject matter of instant claims 1-2, 4 and 6-25 non-statutory under 35 U.S.C. 101 because 35 U.S.C. 101 is drafted in a manner so as to set forth the statutory classes of invention in the alternative only. Please see Ex parte Lyell, 17 USPQ2d 1548 (Bd. Pat. App. & Inter. 1990) Id. at 1551.

To overcome the instant rejection, it is suggested to Applicant to reword the claims to recite the inhibiting properties as a characteristic or a capability of the claimed product. Note that this is a suggestion to overcome the present rejection under 35 U.S.C. 101 and that the adoption of such a suggestion does not necessarily equate to the obviation of any other rejections set forth in the instant Office Action.

This rejection is necessitated by Applicant's amendment to the claims because the present amendment to independent claim 1 now presents the solubilizing 7-ethyl-10-piperidinopiperidinocarbonyloxycamptothecin as an active step of the claimed product, whereas the previously pending claims recited this limitation as a property or characteristic of the claimed product. This newly amended active step of solubilizing is tantamount to a process limitations rather than simply a property or capability of the claimed composition and, thus, renders the instantly amended claims non-statutory pursuant to the provisions of 35 U.S.C. 101 as discussed supra.

For purposes of examination, the claims are interpreted as being drawn to a product.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-2, 4, 6-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chen et al. (U.S. 6,383,471) in view of Li et al. (Am. J. Health-Syst. Pharm. 59, 539-44, 2002).

Chen et al. teaches an aqueous pharmaceutical composition include a hydrophobic therapeutic agent having at least one ionizable functional group and a carrier (abstract and column 34, line 66). The carrier includes an ionizing agent capable of ionizing the functional group, a surfactant, and optionally solubilizers (abstract). Irinotecan is taught to be a hydrophobic therapeutic agent (claim 11). Acetic and ascorbic acid are taught as an ionizing agents to deprotonate the acidic functional group (column 11, lines 21-22). Hydroxypropyl cyclodextrin is taught to be a solubilizer (claim 52). Sodium acetate is taught to be a carrier (Table 20). Propylene glycol is taught to be a surfactant (column 2, lines 7-8).

Chen et al. is silent on an injectable solution having a pH of 2 to 5.

Li et al. teaches an intravenous injectable aqueous pharmaceutical composition comprising irinotecan and phosphoric acid (abstract). Camptothecins, such as irinotecan, are known for their anti-tumor activity (page 539, column 1). Hydrolysis of irinotecan is highly pH dependent with the lowest degradation rate observed in vehicles with a pH of less than 6. Irinotecan should be at a pH of less than 6 (page 541, column 3). The use of a vehicle with a lower pH should help to ensure that a higher concentration of the agent is delivered to the systemic circulation during an infusion (page 543, column 2, last paragraph).

One of ordinary skill in the art would have found it prima facie obvious at the time of the invention to administer the composition as an injection and to maintain a lower pH. One would have been motivated to do so because an aqueous pharmaceutical composition comprising irinotecan is known to be administered via route of injection and further it is known that a lower pH allows for the delivery of a higher concentration of irinotecan in the systemic circulation during infusion.

Additionally, it would have been obvious to vary the amount of different components and ratio between those different components as well as schedule of administration factors that would have been taken into consideration when making such a determination would have included, but not have been limited to, the age, weight, sex, diet and medical condition of the patient, severity of the disease, route of administration, pharmacological considerations, e.g., activity, efficacy, pharmacokinetics and toxicology profiles of the particular compound employed, whether a drug delivery system is utilized and whether the compound is administered as part of a drug combination. Thus, the dosing regimen that would have actually been employed would have expected to vary widely and, in the absence of evidence to the contrary, would have not been inconsistent with that which is presently claimed.

Furthermore, the determination of the optimum pH of the claimed liquid dosage form would also have been a matter well within the purview of the skilled artisan. Such a determination would also have been made in accordance with a variety of factors, such as modifying the pharmaceutical carriers used to

formulate the dosage form to optimize palatability of the dosage form and to maximize tolerability of the composition. In addition, the skilled artisan would also have been motivated to optimize the pH of the solution in order to maintain the active pharmaceutical ingredients in their desired salt form without any degradation of the active ingredients that may occur due to a change in pH.

Conclusion

No claim is found to be allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANNA PAGONAKIS whose telephone number is (571)270-3505. The examiner can normally be reached on Monday thru Thursday, 7am to 5pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brandon Fetterolf can be reached on 571-272-2919. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

AP

/Brandon J Fetterolf/
Supervisory Patent Examiner, Art Unit 1628